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Published in:
Anesthesiology

DOI:
[10.1097/00000542-200607000-00009](https://doi.org/10.1097/00000542-200607000-00009)

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Document Version
Publisher's PDF, also known as Version of record

Publication date:
2006

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Jensen, EW., Litvan, H., Revuelta, M., Rodriguez, BE., Caminal, P., Martinez, P., Vereecke, H., & Struys, M. MRF. (2006). Cerebral state index during propofol anesthesia: A Comparison with the Bispectral Index and the A-Line ARX Index. *Anesthesiology*, 105(1), 28-36. <https://doi.org/10.1097/00000542-200607000-00009>

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Cerebral State Index during Propofol Anesthesia

A Comparison with the Bispectral Index and the A-Line ARX Index

Erik W. Jensen, Ph.D.,* Hector Litvan, M.D., Ph.D.,† Miren Revuelta, M.D.,‡ Bernardo E. Rodriguez, M.Sc.,§ Pere Caminal, Ph.D.,|| Pablo Martinez, M.Sc.,§ Hugo Vereecke, M.D.,# Michel M. R. F. Struys, M.D., Ph.D.**

Background: The objective of this study was to prospectively test the Cerebral State Index designed for measuring the depth of anesthesia. The Cerebral State Index is calculated using a fuzzy logic combination of four subparameters of the electroencephalographic signal. The performance of the Cerebral State Index was compared with that of the Bispectral Index and the A-Line ARX Index.

Methods: This study applied raw data from two previously published clinical protocols. The patients in protocol 1 were given a continuous propofol infusion, 300 ml/h, until 80% of burst suppression occurred. In protocol 2, a stepwise increased target-controlled infusion of propofol was administered to patients until loss of response to noxious stimuli while the Observer's Assessment of Alertness and Sedation was registered every 4 min. The Cerebral State Index was calculated off-line from the recorded electroencephalographic data. The Spearman rank correlation coefficient between electronic indices and the effect site concentration of propofol was calculated along with the prediction probability of each index to predict the Observer's Assessment of Alertness and Sedation level.

Results: The Spearman rank correlation coefficients between the Cerebral State Index, Bispectral Index, and A-Line ARX Index and the propofol effect site concentration were -0.94 , -0.89 , and -0.82 , respectively, in protocol 1, whereas the prediction probability values between the Cerebral State Index, Bispectral Index, and A-Line ARX Index and the Observer's Assessment of Alertness and Sedation score in protocol 2 were 0.92 , 0.93 , and 0.91 , respectively.

Conclusion: The Cerebral State Index detects well the graduated levels of propofol anesthesia when compared with the propofol effect site concentration and the Observer's Assessment of Alertness and Sedation score.

MONITORING depth of anesthesia is gaining increased importance. A number of methods have been suggested, most of them based on the analysis of the electroencephalographic signal. These methods can in general be

classified into those that analyze the spontaneous electroencephalographic activity and those that measure the response of the electroencephalographic signal to acoustic stimuli, auditory evoked potentials (AEPs).

In spontaneous electroencephalogram analysis, initial methods analyzed one single computerized parameter, such as the spectral edge frequency,¹ but during the past decade, a multiparametric approach has been favored in some methods, such as the clustering analysis of subparameters of the electroencephalogram proposed by Thomsen and Prior² or the Bispectral Index (BIS[®]; Aspect Medical Systems, Inc., Newton, MA) validated in numerous publications and calculated by using four subparameters of the electroencephalographic signal.^{3–5}

For the AEP, the particular component that correlates to the depth of anesthesia is the midlatency auditory evoked potential (MLAEP). The MLAEP is allegedly superior to the spontaneous electroencephalographic methods, at least in the early works where the AEP was compared with single parametric analysis of the electroencephalograph.⁶ However, the multiparametric analyses have been shown to have as good a correlation to depth of anesthesia as the MLAEP.^{7–9} Recently, Jensen *et al.*¹⁰ developed a composite index, the A-Line ARX Index, version 1.6 (AAI1.6), based on a combination of MLAEP and spontaneous electroencephalographic data. For the MLAEP part of this algorithm, a previously validated method for fast extraction based on an autoregressive model with an exogenous input adaptive model was used.¹⁰ If the MLAEP quality is too low, spontaneous electroencephalographic components are used. The AAI1.6 is commercially implemented in the AEP Monitor/2 (Danmeter A/S, Odense, Denmark).¹¹

All mentioned derived electroencephalographic and MLAEP indices assume an underlying mathematical function governing the relation between the electroencephalogram and the clinical state of the patient. This might possibly result in less accurate functioning at specific anesthetic states, *e.g.*, causing plateau levels or other less reactive periods in the index at specific levels of the hypnotic component of anesthesia.^{12,13}

A different method for system identification using neural networks and fuzzy logic has been applied increasingly in medical technology, where it provides decision support and expert systems with powerful reasoning capabilities.^{14,15} Fuzzy reasoning allows the implementation of very complex processes, where a simple mathematical model cannot be obtained. Fuzzy logic can also be successfully applied to highly nonlinear processes,

* Research Fellow, Anesthesia Research Group, Department of Cardiac Anesthesia, Hospital de la Santa Creu i Sant Pau, and Biomedical Engineering Research Center, Technical University of Catalonia, Barcelona, Spain. † Chair, ‡ Staff Anesthesiologist, Department of Cardiac Anesthesia and Postoperative Intensive Care Unit, § Research Fellow, Anesthesia Research Group, Department of Cardiac Anesthesia, Hospital de la Santa Creu i Sant Pau. || Professor, Biomedical Engineering Research Center, Technical University of Catalonia, Barcelona, Spain. # Staff Anesthesiologist, Department of Anesthesia, Ghent University Hospital. ** Staff Anesthesiologist, Department of Anesthesia, Ghent University Hospital. Professor in Anesthesia and Research Coordinator, Department of Anesthesia, and Professor in Clinical Pharmacology, Heymans Institute of Pharmacology, Ghent University, Ghent, Belgium.

Received from the Anesthesia Research Group, Department of Cardiac Anesthesia, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain, and the Department of Anesthesia, Ghent University Hospital, Ghent, Belgium. Submitted for publication September 7, 2005. Accepted for publication March 28, 2006. Support was provided solely from institutional and/or departmental sources. Dr. Jensen and Mr. Rodriguez are paid consultants for Danmeter A/S, Odense, Denmark, manufacturer of the Cerebral State Monitor and the AEP Monitor/2.

Address correspondence to Mr. Rodriguez: c/ Joan Coromines 37, 08395 St Pol de Mar, Barcelona, Spain. berodriguez@esteredu.net. Individual article reprints may be purchased through the Journal Web site, www.anesthesiology.org.

where it is observed to greatly simplify the modeling. The advantage of this approach is that it does not assume any underlying mathematical function governing the relation between the electroencephalogram and the clinical state of the patient. It might be hypothesized that this offers modeling advantages because it rather uses clinical data to determine the values of the fuzzy rules to achieve the best fit between the subparameters of the electroencephalogram and the anesthetic depth.

A new index, the Cerebral State Index (CSI), defined by two of the authors (E.W.J. and P.M.), is based on the combination of four subparameters of the electroencephalographic signal. Three of these are derived from spectral analysis of the electroencephalogram, and the fourth is the burst suppression ratio (BS%) calculated by the monitor.

These parameters are used as inputs to an Adaptive Neuro Fuzzy Inference System (ANFIS),^{16,17} which optimizes the rules governing the relation between the input parameters using a least mean squares approach. The mathematics is described in detail in the accompanying appendix. Recently, the CSI has been implemented in a commercially available monitor, the Cerebral State Monitor (Danmeter A/S).

The objective of this study was to prospectively test the correlation of the CSI with the effect site concentration of propofol and with patient state of responsiveness to verbal command as assessed by the Observer's Assessment of Alertness and Sedation (OAA/S) scale. The performance of the CSI was also compared with that of the BIS and AAI indexes in the same patient populations.

Materials and Methods

The raw data from two previously published studies were used. Both patient databases were exclusively obtained at Ghent University Hospital (Gent, Belgium). For all patients in both protocols, informed consent was obtained after approval from the institutional ethics committee.

Protocol 1 studied deep anesthetic levels reaching high levels of burst suppression during propofol administration.¹¹ Protocol 2 studied the correlation between different clinical levels of responsiveness as measured by the OAA/S scale¹⁸ versus the electroencephalogram during steady state propofol administration.⁷ Because the raw electroencephalographic data, vital signs, and pharmacologic data were recorded online and stored electronically in a time-synchronized way, it was possible to reanalyze the raw electroencephalographic data without the requirement of including new patients.

Clinical Protocols

In both protocols, exclusion criteria were weight less than 70% or more than 130% of ideal body weight,

Table 1. Responsiveness Scores of the Modified OAA/S Scale

Score	Responsiveness
5	Responds readily to name spoken in normal tone
4	Lethargic response to name spoken in normal tone
3	Response only after name is called loudly and/or repeatedly
2	Response only after mild prodding or shaking
1	Response only after painful trapezius squeeze
0	No response after painful trapezius squeeze

OAA/S = Observer's Assessment of Alertness and Sedation.

neurologic disorder, and recent use of psychoactive medication, including alcohol.

Protocol 1 (Deep Anesthesia Reaching High Levels of Burst Suppression). The population for this study protocol was formed by 13 patients (10 women, 3 men; American Society of Anesthesiologists physical status I; aged 18–65 yr) scheduled to undergo ambulatory gynecologic or urologic surgery. Before drug administration was started, all patients were asked to close their eyes and relax for 2 min. After this time, baseline measurements were taken. All patients then received a continuous infusion of propofol at 300 ml/h. Infusion was continued until a burst suppression level of 80% or higher was achieved. However, propofol infusion was stopped earlier if the mean arterial blood pressure became lower than 50 mmHg.

Protocol 2 (OAA/S Levels). The study population was formed by 20 female patients (American Society of Anesthesiologists physical status I; aged 18–60 yr) scheduled to undergo ambulatory gynecologic surgery. All patients received an effect site compartment target-controlled infusion of propofol. The initial propofol effect site concentration (C_e prop) was set at 1.5 μ g/ml and increased every 4 min by 0.5 μ g/ml until an OAA/S level of 0 was reached. The level of consciousness, assessed through the OAA/S score, was recorded along with the electronic indices before each increase in effect target concentration. Table 1 describes the OAA/S score levels and their clinical interpretation.

In both protocols, a similar clinical setting was used. Propofol was administered as the only drug, through a large left forearm vein, and infusion was conducted *via* the computer-assisted continuous-infusion device RUG-LOOP II (Demed Engineering, Temse, Belgium). This device drove a Fresenius Modular DPS Infusion Pump connected to a Fresenius Base A (Fresenius Vial Infusion Systems, Brézins, France) through an RS-232 interface. To determine C_e prop, the software uses a three-compartment model enlarged with an effect site compartment, previously published by Schnider *et al.*^{19,20} The calculated C_e prop was computed to yield a time to peak effect of 1.6 min after bolus injection,²¹ as also published by Schnider *et al.*^{19,20} and clinically confirmed by Struys *et al.*²² Heart rate and noninvasive blood pressure, pulse oximetry, and capnography were recorded at 1-min time

intervals using an S5[®] monitor (Datex-Ohmeda, Helsinki, Finland). All patients maintained spontaneous ventilation *via* a facemask delivering 100% oxygen.

Electroencephalographic Measurements

In both protocols, the BIS and the raw electroencephalographic signal with the AEP signal embedded were simultaneously acquired for all patients. The BIS XP[®] (version 4.0) was derived from the frontal electroencephalogram (At-FpzT) and calculated by the A-2000 BIS[®] Monitor using four BIS[®]-Sensor electrodes (Aspect Medical Systems, Inc.). The smoothening time of the BIS[®] monitor was set at 15 s. The raw electroencephalographic signal corresponding to each patient was recorded using the A-Line Monitor (Scientific Version; Danmeter A/S) with three electrodes positioned at midforehead (+), left forehead (reference), and left mastoid (−) along with headphones to deliver a train of bilateral clicks at a frequency of 9 Hz with a 2-ms duration and an adaptable intensity set automatically by the monitor.

The electroencephalographic signal was sampled at 900 Hz and band-pass filtered in the 0.5- to 45-Hz band. The AAI_{1.6} was calculated off-line based on the raw MLAEP data. For all calculations, the AAI has been scaled to a 0–60 interval (AAI₆₀). This scale provides the best stability in the awake state, as proven by Vereecke *et al.*¹¹ The CSI was calculated off-line from the raw electroencephalographic records. Mathematical details from this technology are given in the appendix. It has already been shown that the embedded AEPs resulting from the click stimuli have no effect on the BIS,²³ which includes the β ratio in its calculation. Although an influence of the AEP in the raw signal cannot be excluded, in general, the signal-to-noise ratio between the AEP and the electroencephalographic signal is less than 1 to 30; therefore, the influence of the clicks is assumed to be less than approximately 3% of the final value.

The burst suppression values were taken from the specific parameters calculated by each monitor: the suppression ratio (SR) provided by the BIS and BS% for the AAI₆₀ and CSI calculations.

Statistical Analysis

Comparison between CSI, BIS, and AAI. In protocol 1, a linear regression and its corresponding correlation coefficient was calculated between CSI and BIS. A nonparametric approach, the Spearman rank correlation, *R*, was calculated to study the relation between Ce prop and CSI, BIS, or AAI. The Spearman rank correlation was calculated on pooled data.

The relation between Ce prop and the electroencephalographic measures of anesthetic drug effect was ana-

lyzed using a sigmoid E_{\max} model,

$$\text{Effect} = E_0 + \frac{(E_{\max} - E_0) \times C_{e\gamma}}{(C_{e50\gamma} + C_{e\gamma})},$$

where Effect is the electroencephalographic effect being measured (CSI), E_0 is the baseline measurement when no drug is present, E_{\max} is the maximum possible drug effect, C_e is the calculated effect site concentration of propofol, C_{e50} is the effect site concentration associated with 50% maximal drug effect, and γ is the steepness of the concentration–response relation curve. The model parameters were estimated using NONMEM V (Globomax LLC, Hanover, MD). The parameters for the BIS and AAI₆₀ have already been estimated for this population by Vereecke *et al.*¹¹ The relation between C_e prop and CSI was calculated using the same NONMEM V specifications as described by Vereecke *et al.*¹¹

In protocol 2, the ability of the CSI, BIS, and AAI to predict the response to verbal command, as defined by the OAA/S scale, was evaluated using prediction probability (P_K). Prediction probability was calculated using a custom spreadsheet macro, P_K MACRO, developed by Smith *et al.*^{24,25} The P_K value was calculated as the mean from pooled data of all patients. A P_K of 1 for the CSI indicator would mean that CSI always decreases (increases) as the patient reaches deeper levels of anesthesia according to the OAA/S scale. Such an indicator can perfectly predict the anesthetic state. Alternatively, a P_K value of 0.5 would mean that the indicator is useless for predicting the depth of anesthesia. The jackknife method was used to compute the SE of the estimate.^{24,25} After having evaluated normal distribution, a Student *t* test with Bonferroni correction was used to evaluate significant difference between the P_K means. A Friedman analysis was conducted, and if $P < 0.05$, a Wilcoxon signed rank sum test was used to test for significance between the electronic indices at adjacent OAA/S levels (5 *vs.* 4, 4 *vs.* 3 . . .).

Results

Protocol 1

All data from the published study¹¹ were included in the analysis.

Figure 1 shows a pooled scatter plot of the raw data for all patients. A relation between Ce prop and the electronic indices, CSI, BIS, and AAI₆₀, is hereby shown in plots A, B, and C, respectively. The behavior of the two spontaneous electroencephalographic indices, CSI and BIS, were comparable, as shown in figure 2. The equation for the regression line was $\text{CSI} = 1.02 \text{ BIS}$ ($P < 0.05$ for linearity). Table 2 shows the results of the Spearman rank correlation between propofol and the three indices. The CSI showed a significantly higher correlation than the other two indices.

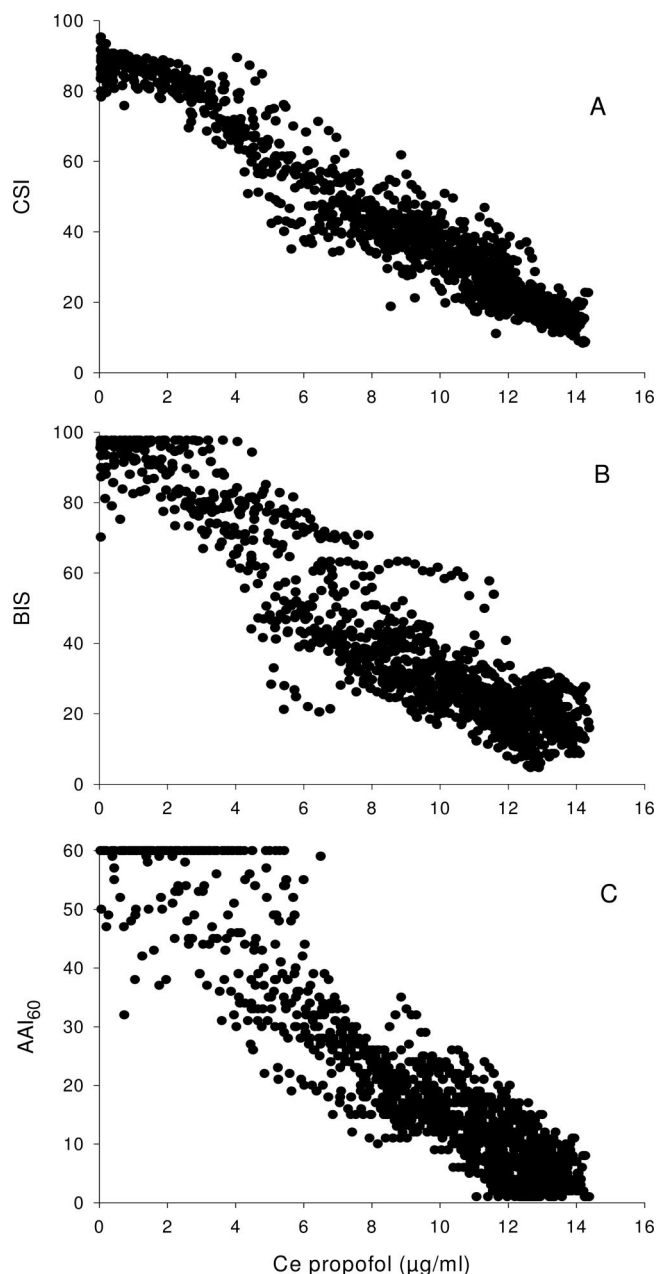


Fig. 1. Raw data of all patients for the three electronic indices (Cerebral State Index [CSI, A]; Bispectral Index [BIS, B]; and A-Line ARX Index version 1.6, scaled to 60 [AAI₆₀, C]) versus propofol effect site concentration (Ce propofol) for the data recorded according to protocol 1.

The high concentrations of propofol caused considerable amount of burst suppression, as shown in figure 3. Figure 3A shows CSI versus its BS%, where the relation is almost linear when BS% is larger than 60. The equation for the regression line, assuming BS% > 1, is shown to have a significant ($P < 0.05$) linear fit to the data. Less linearity is seen for the BIS and AAI₆₀ in figures 3A and B, respectively.

The NONMEM analysis (fig. 4) showed that for this population, the typical values (coefficient of variation) for the sigmoid E_{\max} model between Ce prop and CSI

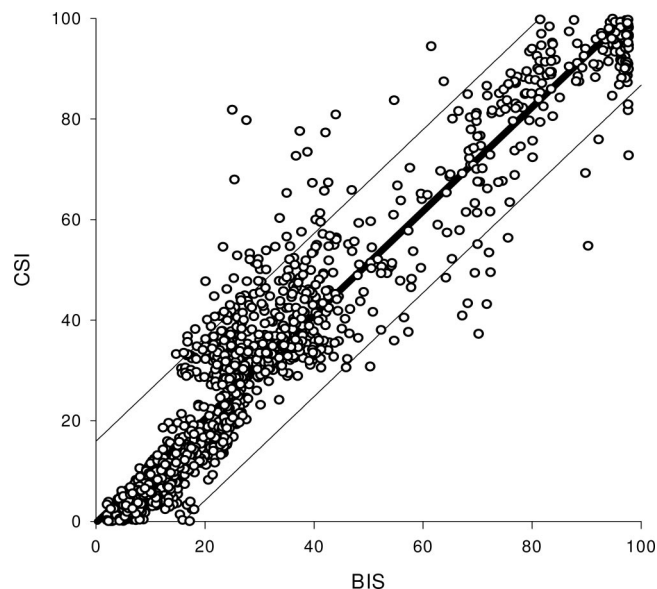


Fig. 2. Linear regression (thick line) and 95% confidence interval (thin lines) between the Cerebral State Index (CSI) and the Bispectral Index (BIS) values for the data recorded according to protocol 1. The regression followed the equation $CSI = 1.02 \text{ BIS}$.

were $C_{50} = 9.85$ (65%), $E_0 = 94$ (4.6%), $E_{\max} = -100$ (110%), and $\gamma = 3.45$ (31%). The SD, depicting the residual intraindividual variability, was 6.79.

Protocol 2

All raw data from the published study were included.⁷ Figure 5 shows the CSI, BIS, and AAI₆₀ versus OAA/S. To compare the different adjacent OAA/S levels for all three indices, a Mann-Whitney U test was applied. The results are shown in table 3. The table shows that in general the BIS and AAI were able to distinguish between OAA/S levels 5 to 2. For the CSI, a smoother drop was observed between level 3 and 2, whereas at deeper anesthesia, the CSI was the only parameter that showed significant differences between OAA/S levels 0 and 1.

Table 4 lists the P_K values of the OAA/S for CSI, BIS, and AAI₆₀. All P_K values were above 0.9, and there were no significant differences between the P_K values of the three electronic indices.

Table 2. Spearman Rank Correlations for the Three Electronic Indices vs. Propofol Effect Site Concentration According to Protocol 1

Index	Spearman Rank Correlation
BIS	-0.818*
AAI ₆₀	-0.887*
CSI	-0.943*

* Correlation is significant at the 0.01 level.

AAI₆₀ = A-Line ARX Index scaled to 60; BIS = Bispectral Index; CSI = Cerebral State Index.

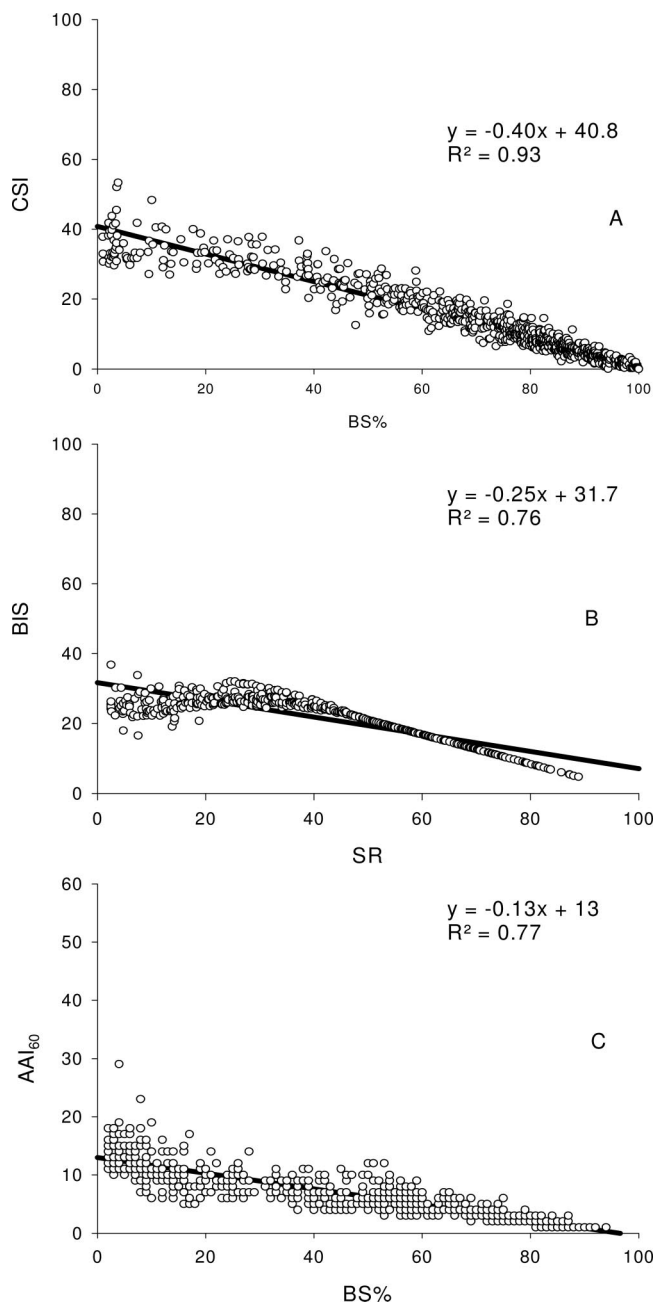


Fig. 3. The relation between the Cerebral State Index (CSI, *A*); Bispectral Index (BIS, *B*); and A-Line ARX Index version 1.6, scaled to 60 (AAI_{60} , *C*), and burst suppression, measured as the burst suppression percentage (BS%) for the CSI and AAI_{60} and as the suppression ratio (SR) for the BIS.

Discussion

The core of the CSI signal processing algorithm is fuzzy logic based. The power of fuzzy logic lies in its ability to perform reasonable and meaningful operations on concepts that cannot be easily codified using a classic logic approach. Such modifications allow for a much more flexible and widespread use of reliable and consistent logic in a variety of applications.

Classic logic relies on something being either true or false. Therefore, either something completely belongs to

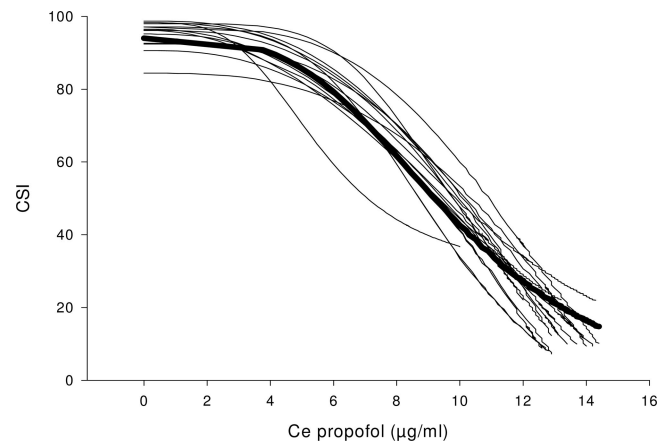


Fig. 4. Sigmoid E_{max} model of the Cerebral State Index (CSI) versus propofol effect site concentration (C_e propofol). The *thin lines* represent individual patient fits, whereas the *bold line* represents the typical curve of the population data.

a set or it is completely excluded from it. Fuzzy logic broadens this definition of membership. The basis of the logic is fuzzy sets. Unlike in “crisp” sets, where membership is full or none, an object is allowed to belong only partly to one set. The membership of an object to a particular set is described by a real value from a range between 0 and 1. Such logic allows a much easier application of many problems that cannot be easily implemented using the classic approach, which only allows a single object to be a member of two mutually exclusive—in the “crisp” sense—sets.

The most common use of fuzzy logic lies in the field of control systems, although the theory seems to have big potential in the different fields of artificial intelligence. The large computational burden of fuzzy logic systems is only justified if a model describing the relation between input and output does not exist. This is the case in the current application, where the relation between the input parameters (β ratio, α ratio, the difference between the two, and BS%) and the clinical state is unknown; therefore, no model is available, which means that the neuro-fuzzy method offers a fast and robust alternative to establish the causal relation between inputs and output. This causal relation may well incorporate nonlinear relations between the linear input parameters, β and α ratio.

When validating a depth of anesthesia monitor, it can only be called accurate if it (1) provides an accurate correlation with cerebral drug effect reflected by its effect site concentration, (2) correlates well with the clinical state of the patients, and (3) informs the clinician when excessive levels of anesthesia are present. In this study, these three aspects were tested using existing databases. The propofol effect site concentration has shown a good correlation to anesthetic depth in several studies, in particular in controlled patient groups; therefore, it was used in this study to evaluate the performance of the CSI as a cerebral drug effect monitor in

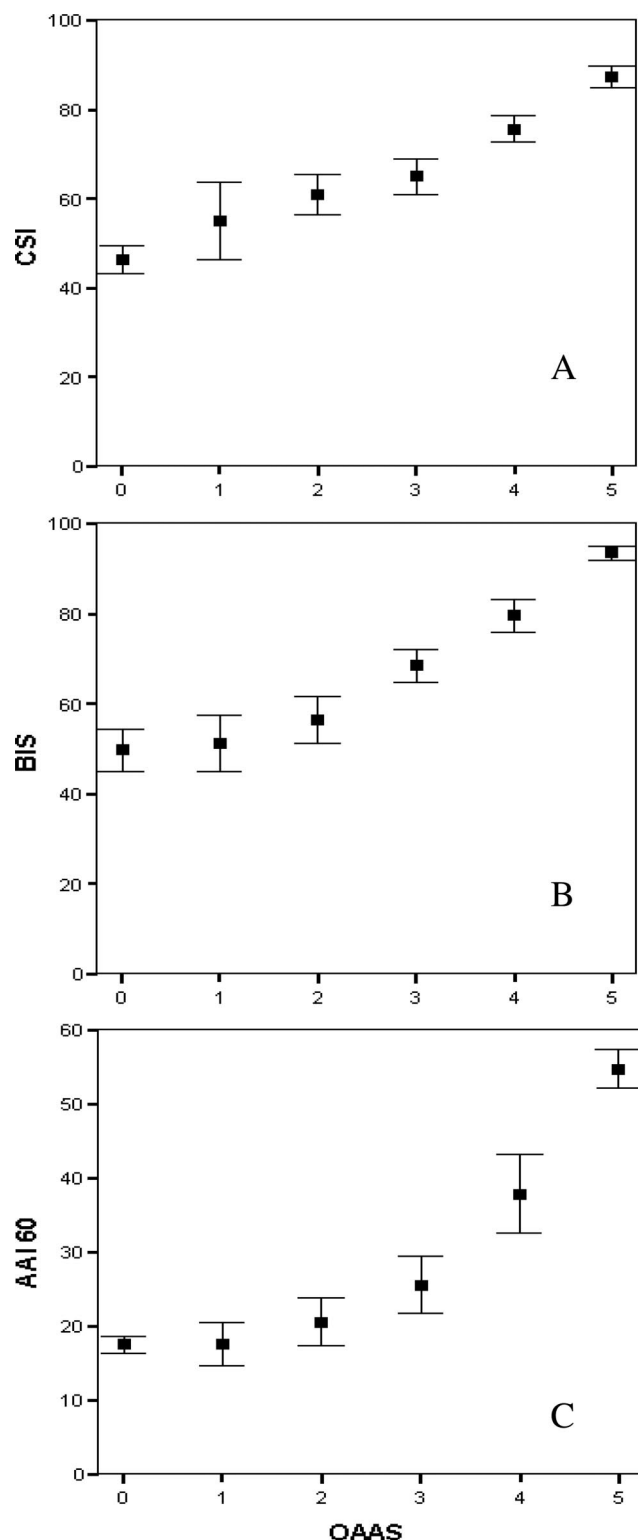


Fig. 5. Mean and 95% confidence interval for Cerebral State Index (CSI, A); Bispectral Index (BIS, B); and A-Line ARX Index version 1.6, scaled to 60 (AAI₆₀, C) versus the Observer's Assessment of Alertness and Sedation Scale (OAA/S), according to protocol 2.

comparison to BIS and AAI₆₀.^{7-9,26} Even more important, a depth of anesthesia monitor should first of all correlate well with the clinical state of the patient, with minimum

Table 3. Mann-Whitney U Test Results (*P* Values) for Significant Differences between the Values of the Three Electronic Indices to Predict Adjacent OAA/S Levels from Protocol 2

OAA/S	BIS	AAI ₆₀	CSI
5 vs. 4	< 0.05	< 0.05	< 0.05
4 vs. 3	< 0.05	< 0.05	< 0.05
3 vs. 2	< 0.05	< 0.05	0.101
2 vs. 1	0.186	0.209	0.257
1 vs. 0	0.530	0.956	< 0.05

All *P* values are two-tailed. *P* < 0.05: significant difference.

AAI₆₀ = A-Line ARX Index scaled to 60; BIS = Bispectral Index; CSI = Cerebral State Index; OAA/S = Observer's Assessment of Alertness and Sedation.

time delay and variation. To investigate this, we selected the OAA/S score because it provides a good correlation with a clinical reflection of the hypnotic component of anesthesia and has been tested prospectively,²⁷ although it has its limitations, as we pointed out in a previous article.²⁸ Burst suppression represents a benign pattern frequently seen in a healthy brain at deep levels of the hypnotic component of anesthesia. It can be identified in the raw electroencephalogram and is composed of episodes of electrical quiescence (the "suppression") alternated with high-frequency, high-amplitude electrical activity (the "bursts"). Increasing anesthetic drug concentration causes increased duration of the suppression periods. Burst suppression patterns of the electroencephalogram are classically quantified as the percentage duration of suppression over a given time period. Because the detection of burst suppression represents an important electroencephalogram component to measure deep levels of anesthesia, its correlation to its univariate parameter is important and must be investigated⁹

The current study demonstrated that both a continuous (protocol 1) and a stepwise increase (protocol 2) in Ce prop resulted in a monotonic decrease in the CSI. These results are comparable with those of our previous study,^{7,8} where it was shown that AAI and BIS decrease during increased Ce prop. In protocol 1, CSI showed the highest correlation to the effect site concentration of propofol. The highest concentration of Ce prop was 14 $\mu\text{g/ml}$ which resulted in CSI values approximately from 10 to 20. The higher correlation might be because the

Table 4. Prediction Probability (*P_K*) for the Electronic Indices to Predict OAA/S Levels from Protocol 2

	<i>P_K</i> for OAA/S Levels
BIS	0.93 (0.01)
AAI ₆₀	0.91 (0.01)
CSI	0.92 (0.01)

Results are shown as mean (SD) jackknife estimate.

AAI₆₀ = A-Line ARX Index scaled to 60; BIS = Bispectral Index; CSI = Cerebral State Index; OAA/S = Observer's Assessment of Alertness and Sedation.

CSI system was partially trained with propofol data, so the pharmacologic relation is already installed in the system. More research must be done to test the behavior of the CSI when other drugs and drug combinations are used. The behaviors of the two indices derived from the spontaneous electroencephalogram, CSI and BIS, are shown in figure 2 to be similar. In this study, a nearly pure linear relation was found between CSI and BIS. Although scientifically not that important, it is interesting from a clinical point of view to have values in the same range with different monitors when indicating identical clinical hypnotic-anesthetic states. Although the overall correlation between CSI and BIS is high, individual variations were present, e.g., a CSI value of 35 simultaneously with a BIS of 70, or *vice versa*, a BIS value of 30 while the CSI was 80. Those individual values are difficult to account for with the current study design; however, it could be due to interference from electromyography in either device. In the awake state, there was a high clustering of data with values of both CSI and BIS above 90. It cannot be ruled out that the CSI has some influence of facialis electromyography. This should be explored in a study where neuromuscular blocking agents are administered.

As said, the behavior of the index at levels of burst suppression was studied. The linear regressions between the indices and their burst suppression shows the highest linearity for CSI, also at low values of BS%, than the corresponding linear regression between BIS and the suppression ratio calculated by the BIS[®] monitor. The relation between BIS and the suppression ratio seems to be biphasic, as published previously,¹¹ which in turn may indicate a better detection of the onset of suppression by the CSI. The AAI₆₀ has less correlation, but monophasic, to the BS% because the BS% has less weight in the AAI algorithm. As shown in figure 5 and table 3, a decrease in the OAA/S score resulted in a monotonic decrease in the three indices, CSI, BIS, and AAI₆₀. A difference between the ability to differentiate the adjacent levels of the OAA/S scale was significant. As seen in previous work,¹¹ BIS and AAI revealed relevant information until loss of consciousness but did not become significant at deeper levels of anesthesia because of the wide variability among patients. The CSI was less significant at the intermediate levels 2 and 3 but was able to distinguish the lowest levels of the OAA/S scale, indicating both loss of responsiveness to verbal and tactile stimuli.

The P_K is widely used to investigate the overall relative performance of the different electroencephalogram-derived indices to measure the hypnotic component of anesthesia.^{24,25} Therefore, P_K analysis was conducted on the study data of protocol 2. Table 4 shows that the CSI has a similar performance to BIS and AAI₆₀ in terms of predicting the clinical state of the patient assessed by the OAA/S scale. Interestingly, the P_K value for AAI₆₀ (0.91),

hereby using the new composite index based on MLAEP and electroencephalographic components, performed somewhat better than the original solitary used fast extracting AEP index (AAI version 1.4, scaled from 0 to 100) as published in the original article⁷ using the same data sets ($P_K = 0.89$).

In conclusion, this study shows that the CSI produces a highly significant correlation with the propofol effect site concentration and has a high P_K for the OAA/S. Further studies are needed to validate the CSI to establish its reliability in clinical practice applying other types of anesthetics and other patient groups.

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Appendix

The CSI

The objective of the Cerebral State Index (CSI) is to monitor the level of consciousness during general anesthesia. The CSI is a unitless scale from 0 to 100, where 0 indicates a flat electroencephalographic signal and 100 indicates the awake state. The range of adequate anesthesia is designed as the 40-60 range (table A1).

The CSI requires three electrodes positioned at the middle forehead, left forehead, and left mastoid. Alternatively, the right forehead and right mastoid can be used.

Methods of the CSI

The CSI is calculated based on four subparameters of the electroencephalogram: β ratio, α ratio, β ratio - α ratio, and burst suppression, defining an index from 0 to 100. The novelty of the CSI is that a fuzzy inference system was used to define the index.

The particular method used was the Adaptive Neuro Fuzzy Inference

Table A1. Definition of CSI Range

CSI	Clinical State
90-100	Awake
80-90	Drowsy
60-80	Light anesthesia or sedation
40-60	Range considered as adequate for surgical anesthesia
10-40	Deep anesthesia, in most cases accompanied by burst suppression
0-10	The BS% is larger than 75. When CSI is below 3, the electroencephalograph is practically isoelectric.

BS% = burst suppression ratio; CSI = Cerebral State Index.

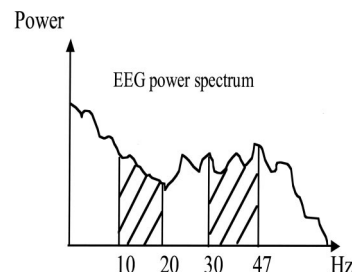


Fig. A1. Power spectrum of the electroencephalographic signal (EEG) showing the bands used for the calculation of the β ratio.

System (ANFIS). The ANFIS was trained with prerecorded electroencephalographic data, where 20 were from propofol and remifentanyl anesthesia, 15 were from propofol infusion until 80% of burst suppression occurred, and 15 were from sevoflurane anesthesia, giving a total of 50 patients. The total number of training points was more than 200,000, sufficient to achieve convergence for the 104 parameters in the 4 input 2 membership ANFIS model. All data were recorded at Gent University Hospital (Ghent, Belgium).

During burst suppression, the α and β ratios are no longer monotonously decreasing as a function of anesthetic depth, and therefore, they cannot be used in the calculation of the final index. Figure A1 shows the power spectrum of the electroencephalographic signal with the bands of the β ratio marked.

The four subparameters were defined as follows:

$$\beta\text{ratio} = \log \frac{E_{30-42.5\text{Hz}}}{E_{11-21\text{Hz}}}$$

$$\alpha\text{ratio} = \log \frac{E_{30-42.5\text{Hz}}}{E_{6-12\text{Hz}}}$$

$$(\beta - \alpha)\text{ratio} = \log \frac{E_{6-12\text{Hz}}}{E_{11-21\text{Hz}}}$$

Burst suppression (BS%): defined as the percentage of time in a 30-s window where the amplitude of the electroencephalographic signal was less than 3.5 μV .

ANFIS Model Structure. Each of the three energy ratios correlates individually to the depth of anesthesia. This has been shown in numerous publications. However, by combining the parameters, a higher correlation coefficient can be reached. An intuitive explanation to this fact is that the ANFIS system, shown in figure A2, automatically uses the best parameter, meaning that when one fails, another might still be a good correlate. The burst suppression parameter indicates deep anesthesia; in this case, the weight on the spectral parameters will be less because they are not good correlates during deep anesthesia with burst suppression due to the nonstationary nature of the electroencephalogram in this situation. The structure of the ANFIS systems ensures that each linguistic term is represented by only one fuzzy set. The parameters of the ANFIS model were determined by training using 50 patients anesthetized with propofol, remifentanyl, and inhalational agents. The total update delay of the index is approximately 15 s.

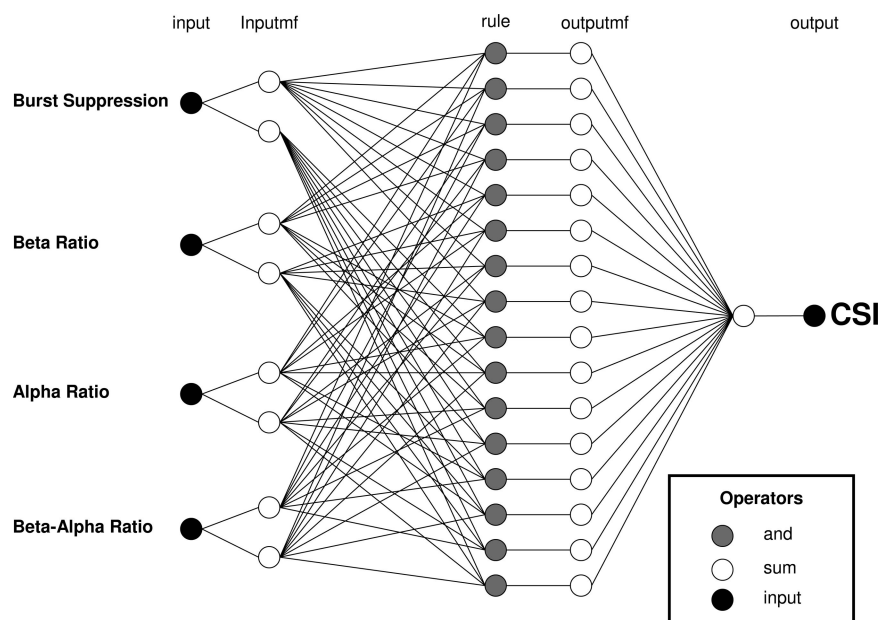


Fig. A2. The Adaptive Neuro Fuzzy Inference System (ANFIS) structure. CSI = Cerebral State Index; inputmf = input membership function; outputmf = output membership function.